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IN THE UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

NYCOMED GMBH, and WYETH Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES, LTD. and TEVA PARENTERAL MEDICINES, INC., Defendants.	Civil Action No.: 08-02877 (JLL)(CCC)

TEVA'S ANSWER

Defendants Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries Ltd., and Teva Parenteral Medicines, Inc. (hereinafter collectively referred to as "Teva"), by its attorneys, hereby answer Plaintiffs' Nycomed Gmbh and Wyeth Complaint as follows:

THE PARTIES

1. Teva is without information sufficient to form a belief as to the truth or falsity of the allegations in ¶ 1 of the Complaint and, therefore, denies the same.

2. Teva is without information sufficient to form a belief as to the truth or falsity of the allegations in ¶ 2 of the Complaint and, therefore, denies the same.

3. Paragraph 3 is not a factual or legal allegation and requires no response.

4. Teva admits that Teva Pharmaceuticals Industries Ltd. ("Teva Industries") is an Israeli corporation having its principal place of business at 5 Bazel, P.O.B. 3190, 49131 Petah Tikva, Israel.

5. Teva admits that Teva Pharmaceuticals USA, Inc. ("Teva USA") is a corporation incorporated under the laws of the State of Delaware and has a place of business at 650 Cathill Road, Sellersville, Pennsylvania 18960, and that it also has a place of businesses at 8-10 Gloria Lane, Fairfield, NJ 07004; but otherwise denies the allegations in ¶ 5 of the Complaint.

6. Teva admits that Teva Parenteral Medicines, Inc. ("Teva Parenteral") is a corporation incorporated under the laws of the State of Delaware, having a place of business at 17 Hughes, Irvine, California, 92618, but otherwise denies the allegations in ¶ 6 of the Complaint.

7. Teva admits that Teva USA is an indirect wholly-owned subsidiary of Teva Industries and that there is limited overlap in the directors and/or officers of the two companies; but otherwise denies the allegations in ¶ 7 of the Complaint.

8. Teva denies the allegations in ¶ 8 of the Complaint.

9. Teva admits that Teva Parenteral is an indirect wholly-owned subsidiary of Teva USA; but otherwise denies the allegations in ¶ 9 of the Complaint.

10. Teva denies the allegations in ¶ 10 of the Complaint.

11. Paragraph 11 is not a factual or legal allegation and requires no response.

JURISDICTION AND VENUE

12. Admitted.

13. Teva admits that Teva USA sells pharmaceuticals throughout the United States, including in New Jersey, of which some products contain materials obtained from Teva Industries. Teva denies the remaining allegations found in ¶ 13 of the Complaint.

14. Admitted.

15. Admitted.

16. With regard to this action, none of the Teva entities challenges personal jurisdiction or venue.

BACKGROUND

17. Upon information and belief, Teva admits that New Drug Application No. 20-988 was approved by the United States Food & Drug Administration for pantoprazole sodium injection 40 mg, which is marketed and sold by Wyeth in the United States under the trade name "PROTONIX® I.V." To the extent not admitted, Teva is without information sufficient to form a belief as to the truth or falsity of the remaining allegations set forth in ¶ 17 and, therefore, denies the same.

18. Teva admits that certain claims of the '579 patent claim a compound that is now commonly known as pantoprazole, which compound is the active ingredient in Plaintiffs' PROTONIX® I.V. product. Teva denies the remaining allegations set forth in ¶ 18 of the Complaint.

19. Teva is without sufficient information to form a belief as to the truth or falsity of the allegations found in ¶ 19 of the Complaint and, therefore, denies the same.

20. Teva admits that a copy of the '579 patent was attached as Exhibit A to the Complaint.

21. Teva admits that Teva Parenteral filed a New Drug Application ("NDA"), No. 22-226, including a certification with respect to the '579 patent under § 505(b)(2)(A)(iv) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) seeking approval to sell pantoprazole sodium injectable 40 mg/vial prior to the expiration of the '579 patent. Teva denies any remaining allegations found in ¶ 21 of the Complaint.

22. Admitted.

23. Teva admits that Teva Parenteral sent a Notice Letter to Nycomed and Wyeth in which Teva represented that it had filed an NDA for pantoprazole sodium injectable 40 mg/vial, including a certification with respect to the '579 patent, and that Teva Parenteral sought approval of its NDA prior to the expiration of the '579 patent. Teva denies any remaining allegations found in ¶ 23 of the Complaint.

24. Teva is without information sufficient to form a belief as to the truth or falsity of the allegations in ¶ 24 of the Complaint and, therefore, denies the same.

25. Teva is without sufficient information to form a belief as to the truth or falsity of the allegations found in ¶ 25 of the Complaint and, therefore, denies the same.

CLAIM FOR RELIEF UNDER 35 U.S.C. § 271(e)

26. Denied.

27. Denied.

28. Denied.

29. Denied.

30. Denied.

PRAYER FOR RELIEF

31. In response to Plaintiffs' prayer for relief in the Complaint:

a. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(a).

b. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(b).

c. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(c).

d. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(d).

e. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(e).

f. Teva denies that Plaintiffs are entitled to the relief requested in ¶ 31(f).

AFFIRMATIVE DEFENSES

FIRST AFFIRMATIVE DEFENSE

32. Teva will not infringe any valid and enforceable claim of the '579 patent under 35 U.S.C. § 271.

SECOND AFFIRMATIVE DEFENSE

33. Upon information and belief, the claims of the '579 patent are invalid under 35 U.S.C. § 103.

THIRD AFFIRMATIVE DEFENSE

34. Upon information and belief, the claims of the '579 patent are invalid under the judicially created doctrine of double patenting in light of U.S. Patent Nos. 4,686,230 and/or 4,555,518.

FOURTH AFFIRMATIVE DEFENSE

35. Upon information and belief, the claims of the '579 patent are unenforceable due to inequitable conduct before the U.S. Patent and Trademark Office.

36. The '579 patent is directed to compounds, including pantoprazole, called proton pump inhibitors (also known as substituted benzimidazoles) used to treat gastrointestinal disorders, such as peptic ulcers, caused by excessive acid production in the stomach.

37. Upon information and belief, the claims of the '579 patent are unenforceable for inequitable conduct because the applicants for the '579 patent, their agents, and others involved in the prosecution of the application for the '579 patent made material misrepresentations to, and withheld material information from, from the U.S. Patent and Trademark Office ("Patent Office") during prosecution of the '579 patent application, related to stability and potency of the compounds, including pantoprazole, claimed in the '579 patent.

38. In an Office Action dated June 10, 1986, the patent examiner examining the application for the '579 patent rejected pending claims 1-19, 21-22, and 24-25 as, *inter alia*, obvious pursuant to 35 U.S.C 103, over either U.S. Patent No. 4,555,518 ("the '518 patent") or U.S. Patent No. 4,560,693 ("the '693 patent") in view of U.S. Patent No. 4,255,431 ("the '431 patent"). The examiner concluded that the only difference between the claimed compounds and the prior art compounds was in the substitution of the pyridine ring of the molecule. Specifically, the only difference was that in either the 3-position or the 5-position of the pyridine ring an alkyl group was changed to an alkoxy group.

39. The examiner further concluded that it would have been obvious to one skilled in the art to interchange an alkoxy group with an alkyl group, based on the '431 patent which teaches such interchangeability.

40. In an Office Action dated, October 28, 1986, the examiner again rejected pending claims 1-19, 21-22, and 24-25, as well as two new claims 26 and 27, as obvious pursuant to 35 U.S.C 103, over the '518 patent or the '693 patent in view of the '431 patent.

41. In an attempt to overcome these obviousness rejections, the patent applicants, in an amendment received by the Patent Office January 27, 1987, argued that the claimed compounds exhibited "unexpected properties" and submitted a declaration under 37 C.F.R 1.132 of Dr. Uwe Kruger ("the First Kruger Declaration"), which contained stability testing data. The purported "unexpected properties" included greater stability (longer half-life) at a pH of 5 over prior art compounds. The compounds were tested in a solution of buffer/acetonitrile at a pH of 5.

42. The patent applicants argued that the purported greater stability of the claimed compounds would result in a reduction of side effects.

43. The patent applicants argued that the test results in the First Kruger Declaration showed "improved chemical stability" of the claimed compounds over the prior art. According to Dr. Kruger, pantoprazole, the only claimed compound at issue in this suit, showed a half-life of greater than 40 hours as compared to a half-life of 5 hours for omeprazole, a prior art compound and the first proton pump inhibitor to enter the marketplace.

44. Despite such purported "unexpected results," the examiner maintained the rejections of the claims based upon the '518 patent and/or the '693 patent in view of the '431 patent. In view of the fact that the '518 and the '693 patents disclosed many compounds nearly identical to all of the claimed compounds, the examiner found the data provided by the applicants insufficient to demonstrate that all of the claimed compounds possessed the purported unexpected properties.

45. The applicants filed a request for reconsideration, but this request was denied.

46. The patent applicants filed a continuation application, dated April 28, 1987, containing a second declaration from Dr. Kruger ("the Second Kruger Declaration"). This declaration contained additional data on additional compounds in an attempt to overcome the examiner's objection as to the scope of the claims. Again, the patent applicants relied upon data derived from testing conducted in a solution of buffer/acetonitrile at a pH of 5 to show purported "unexpected properties" relating to greater stability of the claimed compounds over the prior art. The submitted data indicated that pantoprazole had a half-life of 21 hours, as compared to 5 hours for omeprazole.

47. The examiner again rejected the claims, stating that the applicants had failed to demonstrate unexpected results regarding the primary use of the drugs, namely, the inhibition of gastric acid secretion. The examiner stated that without evidence concerning the relative potencies of the drug, increased stability would not be expected to result in a reduction in side effects.

48. In an amendment dated, February 9, 1988, the applicants submitted three additional declarations (Kruger's Third Declaration, Kruger's Fourth Declaration, and Dr. Konrad Heintze's Declaration) including stability and potency data on additional claimed compounds.

49. Dr. Heintze's Declaration purported to demonstrate that the prior art compounds possessed potency equal to that of the claimed compounds. The examiner required this information in support of the patent applicants' argument that the claimed compounds would lead to a reduction in side effects.

50. Combining this information with all of the Kruger Declarations purporting to show "improved chemical stability," the applicants argued that the claimed compounds, having equal potency but purportedly greater stability than the prior art compounds, were unexpectedly superior to the compounds disclosed in the cited references because they would result in less side effects.

51. The potency data included in Dr. Heintze's Declaration was obtained from a so-called modified Shay-rat testing model. The applicants submitted and relied upon this modified Shay-rat test data in response to the Examiner's request for potency data, but failed to provide the Examiner with information known to them regarding the unreliability of the modified Shay-rat test method in analyzing the potency of proton pump inhibitors.

52. During prosecution of the applications to which the '579 patent claims priority, Altana had patent applications pending in Australia, Application No. 90195/82 ("the Australian Application"), and the European Patent Office, Application 82110054 ("the European Application") for proton pump inhibitors (substituted benzimidazoles that reduce the production of gastric acid). Both the Australian and European Applications contained potency data from modified Shay-rat studies purporting to show the claimed compounds to be superior to the prior art compound omeprazole.

53. Astra, the maker of omeprazole, challenged the modified Shay-rat data by submitting letters to the Australian and European patent offices dated December 6, 1985, and November 29, 1984, respectively. Astra challenged the Shay-rat studies as being unreliable due to a high number of "false positives." Astra cited numerous literature references, including "Gastric Antisecretory Agents," Bristol, J.A. et al., J. Med. Chem., 24 pg. 927-932, 1984, for the

proposition that the Shay-rat test was a test from which "no meaningful structure-activity relationship" could be derived.

54. The literature cited by Astra indicated that the modified Shay-rat tests used and relied upon by Altana resulted in false positives.

55. The literature cited by Astra further indicated that dogs provide a more specific model for testing of the claimed compounds with good correlation to activity in humans than the Shay-rat testing model.

56. Altana abandoned the European Application after Astra's challenge, via a letter dated June 19, 1986.

57. Upon information and belief, Altana abandoned the Australian Application after Astra's challenge.

58. The applicants submitted modified Shay-rat study potency data to the Patent Office during prosecution of the '579 patent, but never disclosed Astra's criticisms, nor the literature cited by Astra, to the Patent Office.

59. The applicants for the '579 patent, their agents, and others involved in the prosecution of the '579 patent knew the reliability of the potency data, or lack thereof, to be material to the examination of the application for the '579 patent, as the Patent Office specifically cited the lack of potency data as part of its grounds for rejecting the claims during prosecution of the '579 patent. The applicants' failure to submit this information was done with the intent to mislead the Patent Office.

60. The patent applicants also intended to mislead the Patent Office by statements made in the specification of the patent at column 1, lines 40-43 stating:

> It has now been found, surprisingly, that the dialkoxypyridines of the present invention have interesting and unexpected properties which advantageously distinguish them from known compounds.

at column 1, lines 62-66 stating:

> A further object is to provide chemically-stable compounds and compositions which have a wide therapeutic range and lack substantial side effects and especially to impart higher chemical stability to pyridylsulfinyl-benzimidazoles.

at column 30, lines 49-51 stating:

> The compounds according to the invention are distinguished by the absence of substantial side effects and by a wide therapeutic range.

and at column 30, lines 63-68 stating:

> Another advantage of the compounds according to the invention is their comparatively high chemical stability.
>
> Surprisingly, the compounds according to the invention are clearly superior (in their excellent properties) to prior art compounds.

61. Upon information and belief, the patent applicants made these statements at a time when they did not possess any data to support these statements. In other words, applicants had no basis to contend that the claimed compounds showed unexpected properties, including greater stability, which would result in fewer side effects.

62. Upon information and belief, Altana did not begin to conduct half-life stability testing at pH 5.0 on the compounds claimed in the '579 patent until long after the application for the '579 patent was filed.

63. Because the applicants for the '579 patent, their agents, and those with a duty of candor to the Patent Office made misleading representations to, and withheld material information from, the Patent Office related to the alleged stability and potency of the compounds

claimed in the '579 patent, including pantoprazole and its salts, the '579 patent is unenforceable due to inequitable conduct committed before the Patent Office.

Dated: August 19, 2008 By: */s/ Michael E. Patunas*

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CERTIFICATION PURSUANT TO L.CIV.R. 11.2

I hereby certify that the matter in controversy is the subject of a related suit involving four of the five parties in the instant suit and involving the same patent. The related suit is *Altana Pharma AG and Wyeth v. Teva Pharmaceuticals USA, Inc. et al.*, Consolidated Civ. Action Nos. 04-2355(JLL), 05-1966 (JLL), 05-3290 (JLL), and 06-3672 (JJL). The parties involved in the related suit are Nycomed GmbH (formerly known as Altana Pharma AG), Wyeth, Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries, Ltd., Sun Pharmaceutical Industries, Ltd., Sun Pharmaceutical Advanced Research Center, Ltd., KUDCo Ireland Limited, and Schwarz Pharma, Inc. The consolidated action is pending in this Court before the Honorable Jose L. Linares.

Dated: August 19, 2008 By: */s/ Michael E. Patunas*

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